REMARKS

Claims 11-25, 27-30, 32-34, and 36-58 remain pending. Applicants note with appreciation that claim 30 has been indicated to contain allowable subject matter. By the foregoing amendment, claims 28 and 29 have been amended to address an issue raised in the Office Action by restating the upper limit of 1.0 wt. % for moxifloxacin, which already appears in independent claim 11. Claims 11 and 28-30 have been amended to clarify that the concentrations refer to weight percent of moxifloxacin, and claims 45-47 and 50 have been amended to correct their dependencies. No new matter is added.

October 16, 2007 Interview

Applicants thank Examiner Fay for the courtesies extended to its representatives Dale H. Hoscheit and Paul M. Rivard during a personal interview on October 16, 2007. During the interview, Applicants' representatives discussed the previously submitted Stroman Declaration and its demonstration of the unexpected ocular penetration properties of pharmaceutical compositions containing moxifloxacin. Examiner Fay agreed the data in the Stroman Declaration demonstrate the non-obviousness of the claimed method for moxifloxacin concentrations up to 0.5 wt. %, but requested further comparative data, particularly for concentrations up to 1.0 wt. %. Such comparative data is provided in the accompanying Owen Declaration and discussed below.

Rejection Under 35 U.S.C. § 112

Claims 28, 29, and 43 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the invention. The Office Action asserts claims 28 and 29 are indefinite for not including an upper limit for the range of

moxifloxacin concentration. However, an upper limit of 1.0 wt. % is stated in independent claim 11, from which claims 28 and 29 depend. In an effort to advance prosecution, claims 28 and 29 have been amended to restate the upper limit of 1.0 wt. % as well.

Claim 43 is alleged to be indefinite for failing to provide sufficient antecedent basis for the limitation "from 0.001 to 1.0 wt. %." Claim 29 (from which claim 43 depends) refers to a moxifloxacin concentration of from 0.35 wt. % to 1.0 wt. %. Claim 43 recites a preservative at a concentration of from 0.001 to 1.0 wt. %, as described in the specification at page 10, lines 1-2. Therefore, there is proper antecedent basis for the preservative concentration range claimed in claim 43. Reconsideration and withdrawal of the rejections under 35 U.S.C. § 112 are respectfully requested.

Rejection Under 35 U.S.C. § 103

Claims 11-29 and 31-58 stand rejected under 35 U.S.C. § 103(a) as being obvious over Petersen et al. U.S. Patent 5,607,942 ("Petersen") in view of Cagle et al. WO 90/01933 ("Cagle '933") and Bergamini et al. U.S. Patent 5,597,560 ("Bergamini"). This rejection is respectfully traversed.

Petersen is cited as describing moxifloxacin in claim 2 and the treatment of eye infections at column 54. Petersen actually discloses well over 100 compounds in Table I and 53 indications in column 54, which amounts to thousands of treatment combinations of quinolone structures and infections. Petersen does not disclose any data whatsoever for moxifloxacin and certainly does not describe or suggest topically applying to the eye a pharmaceutical composition comprising moxifloxacin or a pharmaceutically useful hydrate or salt thereof in a concentration of 0.1 to 1.0 wt. %, as claimed in independent claim 11.

The present record clearly demonstrates the non-obviousness of claim 11 by the superior and unexpected ocular penetration properties exhibited by moxifloxacin compositions. As Dr. Owen states (Owen Dec. ¶ 5), it is widely accepted that ocular penetration properties of fluoroquinolones are best compared under steady state conditions. Fig. 1 of the Owen Declaration is a graph showing *ex vivo* corneal penetration of fluoroquinolones in 0.004 wt. % solutions. It can be readily seen that the moxifloxacin compositions exhibit markedly superior ocular penetration compared to each of the other six fluoroquinolones tested: norfloxacin, ciprofloxacin, gatifloxacin, levoxacin, lomefloxacin, and ofloxacin.

Although Applicants previously demonstrated these unexpected results (Stroman Dec. ¶¶ 17-20), the Office Action asserts the data previously submitted were not commensurate in scope with the claims. In particular, the Examiner has requested comparative testing at the upper end of the concentration range. Such testing is described in the attached Owen Declaration in response to the Examiner's request.

As described in the specification, ophthalmic formulations should be formulated to have a pH specially suited for application to ophthalmic tissues. Ideally, the solutions are prepared at or near physiological pH, i.e., approximately 7.2 – 7.3. However, because of the relatively low solubility of some fluoroquinolones, solutions of higher concentrations, e.g., 0.5 – 1.0 wt.%, could not be prepared at pH 7.2 – 7.3. Therefore, to accommodate the Examiner's request for comparative testing at the upper end of the concentration range, it was necessary to lower the pH for certain comparative fluoroquinolone solutions.[1] For example, pH was adjusted to 5.8 to permit a 1.0 wt. % solution of ofloxacin to be prepared. (Owen Dec. ¶ 9).

[1] Moxifloxacin solutions also were prepared and tested at the corresponding (lowered) pH conditions as reported in the Owen Declaration (see ¶ 9). Such acidic pH conditions are not optimally suited for moxifloxacin ophthalmic solutions. Therefore, the more meaningful comparisons of moxifloxacin and other quinolone ophthalmic solutions are those involving compositions formulated as near as practicable to physiologic pH (approximately pH 7.3).

Tables 2A, 2B, 2C, and 2D and Figures 2A, 2B, 2C, and 2D in the Owen Declaration show the results of *ex vivo* corneal perfusion chamber rates of diffusion of moxifloxacin, ofloxacin, lomefloxacin, gatifloxacin, ciprofloxacin, and levoxacin in 0.1, 0.3, 0.5, and 0.75 wt. % solutions, respectively. Table 2E and Figure 2E show *ex vivo* corneal perfusion chamber rates of diffusion (flux) of moxifloxacin, ofloxacin, levoxacin, and gatifloxacin in 1.0 wt. % solutions.[2] At each concentration over the range of 0.1 to 1.0 wt. %, the "results clearly demonstrate the significantly superior corneal penetration properties exhibited by moxifloxacin compositions over compositions containing the other tested fluoroquinolones." (Owen Dec. ¶¶ 9-10). In addition, *in vivo* testing in a rabbit model further confirmed that "moxifloxacin compositions exhibited superior ocular penetration properties compared to ofloxacin compositions" at concentrations of 0.5, 0.75 and 1.0 wt. %. (Owen Dec. ¶¶ 11-12; Tables 3A-3B; Figures 3A-3B).

The Owen Declaration demonstrates the unexpectedly superior ocular penetration of moxifloxacin compositions over all other fluoroquinolones tested throughout the 0.1 – 1.0 wt. % concentration range of independent claim 11. The overwhelming evidence of unexpected results in the Owen Declaration, taken together with the other evidence of record, compels a conclusion of non-obviousness of independent claim 11.

The secondary references to Cagle '933 and Bergamini are cited as describing the use of steroidal and non-steroidal anti-inflammatory agents in ophthalmic formulations, respectively. Cagle '933 and Bergamini fail to disclose or suggest the presently claimed use of moxifloxacin and fail to remedy the deficiencies of Petersen as discussed above. Nothing in the Cagle '933 and Bergamini references would lead a person of ordinary skill in the art to select moxifloxacin

[2] 1.0 wt.% solutions of ciprofloxacin and lomefloxacin were not prepared because the pH required for such solutions would be expected to result in corneal damage to the rabbit lens used in the model.

from the many compounds disclosed in Petersen, and nothing in those references would give such a person any reason to expect that the use of moxifloxacin as presently claimed would yield the superior penetration demonstrated in the Owen Declaration. Dependent claims 12-25, 27-29, 32-34, and 36-58 are allowable over Petersen, Cagle '933, and Bergamini for at least the same reasons as argued above.

CONCLUSION

In view of the foregoing, favorable reconsideration and allowance of the subject application are respectfully requested.

Respectfully submitted,

BANNER & WITCOFF, LTD.

Date: February 27, 2008

By: /Paul M. Rivard/
Paul M. Rivard
Registration No. 43,446

1100 13th Street N.W.
Suite 1200
Washington, DC 20005-4051
(202) 824-3000 (telephone)
(202) 824-3001 (facsimile)